09/368,076

	L #	Hits	Search Text	DBs	Time Stamp
1	L1	448	435/236.ccls.	USPAT	2001/07/18 12:24
2	L2	291	435/237.ccls.	USPAT	2001/07/18 12:25
3	L3	251	435/238.ccls.	USPAT	2001/07/18 12:25
4	L4	529	424/93.2.ccls.	USPAT	2001/07/18 12:25
5	L5	268	424/199.1.ccls.	USPAT	2001/07/18 12:25
6	L6	87	424/205.1.ccls.	USPAT	2001/07/18 12:25
7	L7	100	424/211.1.ccls.	USPAT	2001/07/18 12:25
8	L8	1577	1 or 2 or 3 or 4 or 5 or 6 or 7	USPAT	2001/07/18 12:26
9	L9	1068	respiratory adj syncytial adj virus	USPAT	2001/07/18 12:26
10	L10	136	8 and 9	USPAT	2001/07/18 12:26
11	L11	22293	m2	USPAT	2001/07/18 12:26
12	L12	27800	sh	USPAT	2001/07/18 12:26
13	L13	805	ns1	USPAT	2001/07/18 12:26
14	L14	415	ns2	USPAT	2001/07/18 12:27
15	L16	50251	11 or 12 or 13 or 14	USPAT	2001/07/18 12:27
16	L17	26	10 and 16	USPAT	2001/07/18 12:28

Set	Items	Description
S1	29592	RESPIRATORY(W)SYNCYTIAL(W)VIRUS
S2	26684	RSV
S3	45175	S1 OR S2
S4	134931	SH
S5	8818	NS1
S6	3341	NS2
S7	1465647	MUTATED OR MUTATION OR DELETED OR DELETION
S8	2652	M2(W)2
S9	23	M2(W)ORF2
S10	2669	S8 OR S9
S11	571	S3 AND S4 AND S7
S12	239	S11 NOT PY>1998
S13	219	RD (unique items)
S14	18727	S3/TI
S15	9	S13 AND S14
S16	40	S14 AND S5 AND S7
S17	7	S16 NOT PY>1998
S18	7	RD (unique items)
S19	31	S14 AND S6 AND S7
S20	5	S19 NOT PY>1998
S21	5	RD (unique items)
S22	37	S14 AND S10 AND S7
S23	3	S22 NOT PY>1998
S24	3	RD (unique items)
S25	8716648	REPLICATE OR REPLICATION OR INFECTION OR INFECTED OR GROW - OR GROWTH
S26	147770	S4 OR S5 OR S6 OR S10
S27	331	S14 AND S25 AND S26
S28	125	RD (unique items)
S29	71	S28 NOT PY>1998
S30	1130	AU="JIN H"
S31	354	AU="JIN H."
S32	83	AU="JIN HONG"
S33	428	AU="TANG R"
S34	163	AU="TANG R."
S35	12	AU="TANG RODERICK" OR AU="TANG RODERICK S"
S36	79	AU="LI SHENG"
S37	256	AU="BRYANT M"
S38	65	AU="BRYANT MARTIN" OR AU="BRYANT MARTIN L"
S39	2540	S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38
S40	31	S3 AND S39
S41	17	RD (unique items)

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29/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09776202 98285727 PMID: 9621029
Identification of the respiratory syncytial virus **proteins required for formation and passage of helper-dependent infectious particles.**
Teng MN; Collins PL
Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland 20892-0720, USA.
Journal of virology (UNITED STATES) Jul 1998, 72 (7) p5707-16, ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We developed a system to identify the viral proteins required for the packaging and passage of human respiratory syncytial virus (RSV) by reconstructing these events with cDNA-encoded components. Plasmids encoding individual RSV proteins, each under the control of a T7 promoter, were cotransfected in various combinations together with a plasmid containing a minigenome into cells **infected** with a vaccinia virus recombinant expressing T7 RNA polymerase. Supernatants from these cells were passaged onto fresh cells which were then superinfected with RSV. Functional reconstitution of RSV-specific packaging and passage was detected by expression of the reporter gene carried on the minigenome. As expected, the four nucleocapsid proteins N, P, L, and M2-1 failed to direct packaging and passage of the minigenome. Passage was achieved by further addition of plasmids expressing three membrane-associated proteins, M, G, and F; inclusion of the fourth envelope- associated protein, **SH** , did not alter passage efficiency. Passage was reduced 10- to 20-fold by omission of G and was abrogated by omission of either M or F. Coexpression of the nonstructural **NS1** or **NS2** protein had little effect on packaging and passage except through indirect effects on RNA synthesis in the initial transfection. The M2-1 transcription elongation factor was not required for the generation of passage-competent particles. However, addition of increasing quantities of M2-1 to the transfection mediated a dose-dependent inhibition of passage which was alleviated by coexpression of the putative negative regulatory factor **M2 - 2** . Omission of the L plasmid reduced passage 10- to 20-fold, most likely due to reduced availability of encapsidated minigenomes for packaging. However, the residual level of passage indicated that neither L protein nor the process of RSV-specific RNA synthesis is required for the production and passage of particles. Omission of N or P from the transfection abrogated passage. Thus, the minimum RSV protein requirements for packaging and passaging a minigenome are N, P, M, and F, although the efficiency is greatly increased by addition of L and G.

29/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09646998 98105793 PMID: 9445048
The NS1 **protein of human** respiratory syncytial virus **is a potent inhibitor of minigenome transcription and RNA** replication.
Atreya PL; Peeples ME; Collins PL
Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892-0720, USA.
Journal of virology (UNITED STATES) Feb 1998, 72 (2) p1452-61,

ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

The **NS1** protein (139 amino acids) is one of the two nonstructural proteins of human respiratory syncytial virus (RSV) and is encoded by a very abundant mRNA transcribed from the promoter-proximal RSV gene. The function of **NS1** was unknown and was investigated here by using a reconstituted transcription and RNA **replication** system that involves a minireplicon and viral proteins (N, P, L and M2-1) expressed from separate cotransfected plasmids. Coexpression of the **NS1** cDNA strongly inhibited transcription and RNA **replication** mediated by the RSV polymerase, even when the level of expressed **NS1** protein was substantially below that observed in RSV-**infected** cells. The effect depended on synthesis of **NS1** protein rather than **NS1** RNA alone. Transcription and both steps of RNA **replication** , namely, synthesis of the antigenome and the genome, appeared to be equally sensitive to inhibition. The efficiency of encapsidation of the plasmid-derived minigenome was not altered by coexpression of **NS1** , indicating that the inhibition occurs at a later step. In two different dicistronic minigenomes, transcription of each gene was equally sensitive to inhibition by **NS1** . This suggested that the gradient of transcriptional polarity was unaffected and that the effect of **NS1** instead probably involves an early event such as polymerase entry on the genome. **NS1** -mediated inhibition of transcription and RNA **replication** was not affected by coexpression of the M2 mRNA, which has two open reading frames encoding the transcriptional elongation factor M2-1 and the putative negative regulatory factor **M2** - **2** . The potent nature of the **NS1** -mediated inhibition suggests that negative regulation is an authentic function of the **NS1** protein, albeit not necessarily the only one.

29/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09612997 98054343 PMID: 9391135

Respiratory syncytial virus (RSV) SH **and G proteins are not essential for viral** replication **in vitro: clinical evaluation and molecular characterization of a cold-passaged, attenuated** RSV **subgroup B mutant.**

Karron RA; Buonagurio DA; Georgiu AF; Whitehead SS; Adamus JE; Clements-Mann ML; Harris DO; Randolph VB; Udem SA; Murphy BR; Sidhu MS
Center for Immunization Research, Department of International Health, School of Hygiene and Public Health, The Johns Hopkins University, Baltimore, MD 21205, USA. rkarron@jhsph.edu

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Dec 9 1997, 94 (25) p13961-6, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: AI-15095, AI, NIAID
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

A live, cold-passaged (cp) candidate vaccine virus, designated respiratory syncytial virus (RSV) B1 cp-52/2B5 (cp-52), replicated efficiently in Vero cells, but was found to be overattenuated for RSV-seronegative infants and children. Sequence analysis of reverse-transcription-PCR-amplified fragments of this mutant revealed a large deletion spanning most of the coding sequences for the small hydrophobic (**SH**) and attachment (G) proteins. Northern blot analysis of cp-52 detected multiple unique read-through mRNAs containing **SH** and G sequences, consistent with a deletion mutation spanning the **SH** :G gene

junction. Immunological studies confirmed that an intact G glycoprotein was not produced by the cp-52 virus. Nonetheless, cp-52 was infectious and replicated to high titer in tissue culture despite the absence of the viral surface **SH** and G glycoproteins. Thus, our characterization of this negative-strand RNA virus identified a novel **replication** -competent deletion mutant lacking two of its three surface glycoproteins. The requirement of **SH** and G for efficient **replication** in vivo suggests that selective deletion of one or both of these RSV genes may provide an alternative or additive strategy for developing an optimally attenuated vaccine candidate.

29/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09058317 97017588 PMID: 8864205
Expression and characterisation of the NS1 **and** NS2 **proteins of** respiratory syncytial virus.
Evans JE; Cane PA; Pringle CR
Department of Biological Sciences, University of Warwick, Coventry, UK.
Virus research (NETHERLANDS) Aug 1996, 43 (2) p155-61, ISSN 0168-1702 Journal Code: X98
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The **NS1** and **NS2** proteins of human respiratory syncytial virus (RSV) were expressed using baculovirus. Antisera to these expressed proteins and to synthetic peptides were raised in rabbits and used to characterise the proteins. Multiple forms of both **NS1** and **NS2** proteins were detected in RSV **infected** cells by both immunoblotting and radioimmunoprecipitation when non-reducing, but not reducing, conditions were used. In pulse-labelling experiments the monomeric form of **NS1** was stable, while that of **NS2** was unstable with a half life of about 30 min. The **NS1** protein associated with the matrix (M) protein and could be co-precipitated by a monoclonal antibody to M protein. The **NS2** protein did not show any detectable association with RSV structural proteins. These results indicate that the **NS1** and **NS2** proteins have distinct roles in the viral life cycle.

29/3,AB/52 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0157084 DBA Accession No.: 93-15136 PATENT
Cold-adapted mutant respiratory- syncytial virus - **attenuation and antigen gene cloning for use as a recombinant vaccine**
PATENT ASSIGNEE: Am.Cyanamid 1993
PATENT NUMBER: EP 567100 PATENT DATE: 931027 WPI ACCESSION NO.: 93-338162 (9343)
PRIORITY APPLIC. NO.: US 871420 APPLIC. DATE: 920421
NATIONAL APPLIC. NO.: EP 93106496 APPLIC. DATE: 930421
LANGUAGE: English
ABSTRACT: A cold-adapted attenuated mutant respiratory-syncytial virus (RSV) of subgroup A or B is new, e.g. virus 3Ap20E, 3Ap20F, 3Ap28F, 2Bp33F, 2Bp24G, 2Bp20L or 2Bp34L. A purified immunogenic polypeptide (e.g. specified polypeptides L, F, G, M, M2(22K), P, **SH** , 1B, 1C or N) is also new, as is nucleic acid encoding the RSV polypeptides. The virus, polypeptides and nucleic acids are useful in recombinant vaccines against RSV **infection** . In preferred embodiments, plasmid,

vaccinia virus, polio virus, adeno virus and baculo virus vectors for RSV protein gene cloning are described. An RSV polypeptide gene may be inserted into such a vector with specific initiation signals and transcription-translation control signals and a selectable marker and expressed in e.g. a CHO cell culture, insect cell culture, Escherichia coli, Salmonella sp. or Shigella sp. for recombinant vaccine production. The recombinant RSV polypeptide may be purified by chromatography, centrifugation, precipitation, etc. (63pp)

29/3,AB/60 (Item 3 from file: 349)
DIALOG(R)File 349:PCT Fulltext

00537299
ATTENUATED RESPIRATORY SYNCYTIAL VIRUS
VIRUS RESPIRATOIRE SYNCYTIAL ATTENUE
Patent Applicant/Assignee:
THE REGENTS OF THE UNIVERSITY OF MICHIGAN, THE REGENTS OF THE UNIVERSITY OF MICHIGAN , Management Technology Office, Wolverine Tower, Room 2071, 3003 South State Street, Ann Arbor, MI 481091280 , US
Inventor(s):
MAASSAB Hunein F, MAASSAB, Hunein, F. , 2446 Shannondale, Ann Arbor, MI 48104 , US
HERLOCHER M Louise, HERLOCHER, M., Louise , 2142 Spruceway Lane, Ann Arbor, MI 48103 , US
Patent and Priority Information (Country, Number, Date):
Patent: WO 9738138 A1 19971016
Application: WO 97US5588 19970403 (PCT/WO US9705588)
Priority Application: US 9614848 19960404
Designated States: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU GH KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
Publication Language: English
Filing Language: English
Fulltext Word Count: 12738

English Abstract
Attenuated respiratory syncytial viruses (RSV) and in particular temperature sensitive RSV are provided. The viruses of the present invention may be used in pharmaceutical compositions such as vaccines. Methods of making and using such pharmaceutical compositions are also provided.

French Abstract
On decrit des virus respiratoires syncytiaux (RSV) attenues et notamment de tels virus sensibles a la temperature. On peut utiliser les virus de la presente invention dans des compositions pharmaceutiques telles que des vaccins. On decrit egalement des procedes de preparation et d'utilisation de telles compositions pharmaceutiques.
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41/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10687850 20351739 PMID: 10891423
Recombinant respiratory syncytial viruses with deletions in the NS1, NS2, SH, and M2-2 genes are attenuated in vitro and in vivo.
Jin H ; Zhou H; Cheng X; **Tang R** ; Munoz M; Nguyen N
Aviron, 297 North Bernardo Avenue, Mountain View, California, 94043, USA. hjin@aviron.com
Virology (UNITED STATES) Jul 20 2000, 273 (1) p210-8, ISSN 0042-6822 Journal Code: XEA
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Respiratory syncytial virus (**RSV**) encodes several proteins that lack well-defined functions; these include NS1, NS2, SH, and M2-2. Previous work has demonstrated that NS2, SH, and M2-2 can each be deleted from **RSV** genome and thus are considered as accessory proteins. To determine whether **RSV** can replicate efficiently when two or more transcriptional units are deleted, we removed NS1, NS2, SH, and M2-2 genes individually and in different combinations from an infectious cDNA clone derived from human **RSV** A2 strain. The following six mutants with two or more genes deleted were obtained: DeltaNS1NS2, DeltaM2-2SH, DeltaM2-2NS2, DeltaSHNS1, DeltaSHNS2, and DeltaSHNS1NS2. Deletion of M2-2 together with NS1 was detrimental to **RSV** replication. It was not possible to obtain a recombinant **RSV** when all four genes were deleted. All of the double and triple deletion mutants exhibited reduced replication and small plaque morphology in vitro. Replication of these deletion mutants was more reduced in HEp-2 cells than in Vero cells. Among the 10 single and multiple gene deletion mutants obtained, DeltaM2-2NS2 was most attenuated. DeltaM2-2NS2 formed barely visible plaques in HEp-2 cells and had a reduction of titer of 3 log(10) compared with the wild-type recombinant **RSV** in infected HEp-2 cells. When inoculated intranasally into cotton rats, all of the deletion mutants were attenuated in the respiratory tract. Our data indicated that the NS1, NS2, SH, and M2-2 proteins, although dispensable for virus replication in vitro, provide auxiliary functions for efficient **RSV** replication. Copyright 2000 Academic Press.

41/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10436423 20057898 PMID: 10590093
Respiratory syncytial virus **that lacks open reading frame 2 of the M2 gene (M2-2) has altered growth characteristics and is attenuated in rodents.**
Jin H ; Cheng X; Zhou HZ; Li S; Seddiqui A
Aviron, Mountain View, California 94043, USA. hjin@aviron.com
Journal of virology (UNITED STATES) Jan 2000, 74 (1) p74-82, ISSN 0022-538X Journal Code: KCV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The M2 gene of **respiratory syncytial virus** (**RSV**) encodes two putative proteins: M2-1 and M2-2; both are believed to be involved in the RNA transcription or replication process. To understand the function of the M2-2 protein in virus replication, we deleted the majority of the M2-2 open reading frame from an infectious cDNA clone derived from the human **RSV** A2

strain. Transfection of HEp-2 cells with the cDNA clone containing the M2-2 deletion, together with plasmids that encoded the **RSV** N, P, and L proteins, produced a recombinant **RSV** that lacked the M2-2 protein (rA2DeltaM2-2). Recombinant virus rA2DeltaM2-2 was recovered and characterized. The levels of viral mRNA expression for 10 **RSV** genes examined were unchanged in cells infected with rA2DeltaM2-2, except that a shorter M2 mRNA was detected. However, the ratio of viral genomic or antigenomic RNA to mRNA was reduced in rA2DeltaM2-2-infected cells. By use of an antibody directed against the bacterially expressed M2-2 protein, the putative M2-2 protein was detected in cells infected with wild-type **RSV** but not in cells infected with rA2DeltaM2-2. rA2DeltaM2-2 displayed a small-plaque morphology and grew much more slowly than wild-type **RSV** in HEp-2 cells. In infected Vero cells, rA2DeltaM2-2 exhibited very large syncytium formation compared to that of wild-type recombinant **RSV** . rA2DeltaM2-2 appeared to be a host range mutant, since it replicated poorly in HEp-2, HeLa, and MRC5 cells but replicated efficiently in Vero and LLC-MK2 cells. Replication of rA2DeltaM2-2 in the upper and lower respiratory tracts of mice and cotton rats was highly restricted. Despite its attenuated replication in rodents, rA2DeltaM2-2 was able to provide protection against challenge with wild-type **RSV** A2. The genotype and phenotype of the M2-2 deletion mutant were stably maintained after extensive in vitro passages. The attenuated phenotype of rA2DeltaM2-2 suggested that rA2DeltaM2-2 may be a potential candidate for use as a live attenuated vaccine.
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